Genetic diversity of 100+ Aspergillus species: The aspMine analysis resource

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Total number of authors:
16

Publication date:
2017

Document Version
Publisher's PDF, also known as Version of record

Genetic diversity of 100+ Aspergillus species

The aspMine analysis resource

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Curious about the Aspmine? Ask me!

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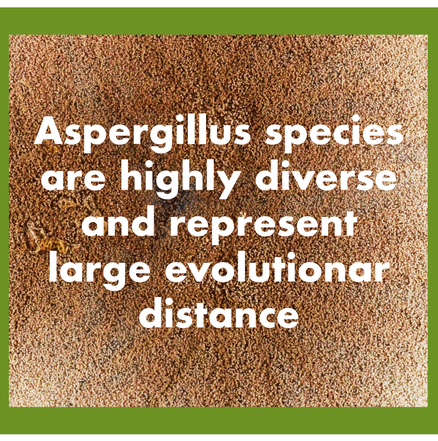
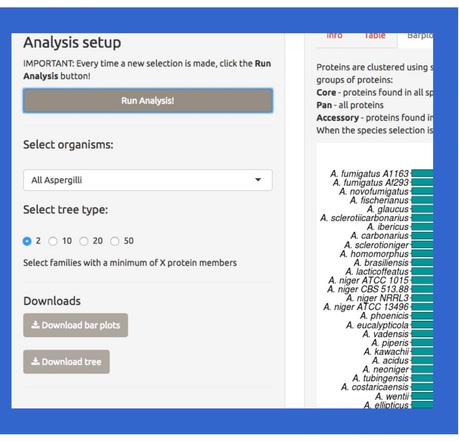
Background



Interactive analysis apps

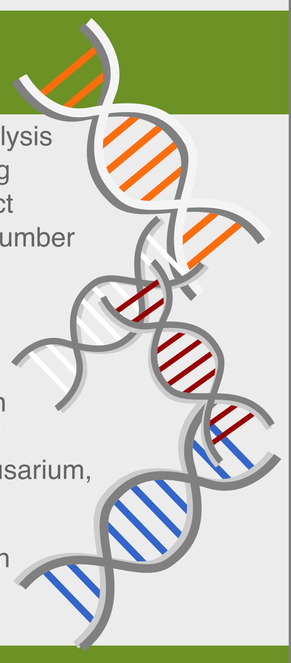
- The aspmine is a webpage
- Contains documentation of analysis
- Holds link to interactive analysis apps
- Apps allow the user to explore the analysis data
- Figures and tables are available for download
- Analysis in the apps can be customized by selecting organisms of interest and cutoffs or subsets of data



Fungi

- Producers of chemically and medically relevant compunds
- Large natural diversity and high production of bioactive compounds
- Well studied production organisms
- Can be genetically optimized for production of cheeper and environmentally friendly compounds

Sequencing



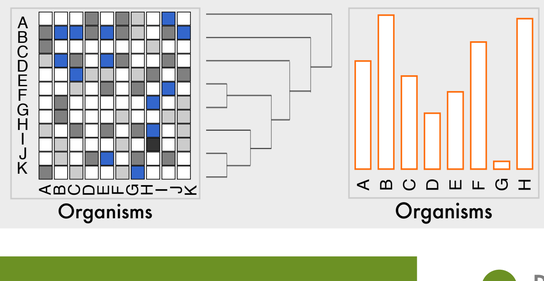
Genome sequencing and analysis can elucidate many interesting genetic features. In this project we aim to sequence a large number of Aspergillus species

- Initiative to sequence > 300 species
- DTU IBT Culture Collection > 35,000 fungal cultures of Penicillium, Aspergillus, Fusarium, Alternaria and Tricoderma
- Data represents 200 million years of evolution

Comparative Genomics

Comparative genomics can be used to investigate a number of aspects of genetic diversity. Here we focus on evolutionary development of Aspergillus species and diversity of secondary metabolism

- Genomes/annotation measures and quality
- Genetic diversity of Aspergilli
- Families of proteins with shared functions
- Genes/proteins specific to single species
- Shared protein families within groups of species
- Horizontal gene transfers across large phylogenetic distances
- Families of secondary metabolism gene clusters responsible for similar compounds



Analysis setup

Analysis database - the workhorse

- Relational databases are ideal for combining different data types as well as conditional selction of data
- Raw data is obtained from JGI and is stored in a costume designed relational database (MySQL)
- Data include functional annotation and protein sequences
- All proteins are compared across the growing dataset (BLAST)
- BLAST alignement scores are stored in the database

Raw information
- Taxonomical section
- Protein sequences
- Organism name and ID

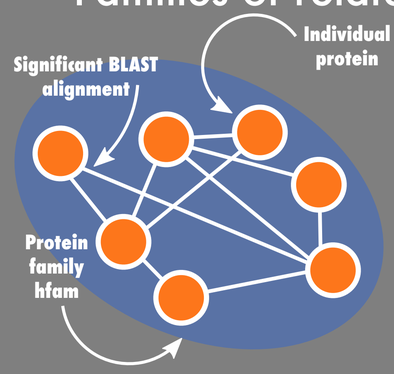
Functional annotation
- SMURF - secondary metabolism
- InterPro - domains
- KOG - kategories
- KEGG - pathways

BLAST alignment data
- Query/hit coverage
- Alignment coverage
- Percent identity
- Reciprocal hit flag

Selecting data conditionally

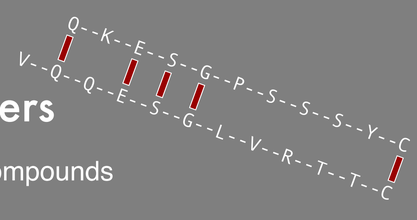
- MySQL is ideal for extracting data which fulfills specific criteria
- Examples of conditonal selection of data in the analysis database
  - Genes found only in a subset of species
  - Specific functional annotation which i always found twice in Aspergilli
  - Genes containing signal peptides and found in a specific set of species

Families of related proteins - aspmine hfams



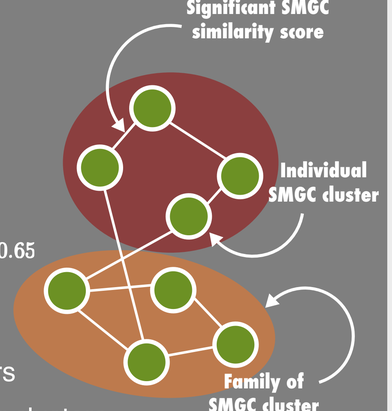
- Assumption: similar protein sequences imply similar function
- Sequence similarity can be defined by alignments
- Alignements are determined using BLAST
- Alignement coverage of hit plus query must be over 130%
- Identical resedues in alignment must be over 50%
- Proteins are connected using single linkage, a protein need only be connected to one other memeber of the cluster.

Families of related SMGCs - Secondary Metabolism Gene Clusters



- Assumption: SMGCs with similar genes will create similar compounds
- Functionally similar genes can be identified using BLAST
- Enzymes that initiate a secondary metabolite (backbones) are most important in the definition of that metabolite
- Tailoring enzymes also hold information about the metabolite but to a lesser extend than backbone enzymes
- SMGCs must share a significant fraction of backbone and tailoring enzyme activities to create similar compounds

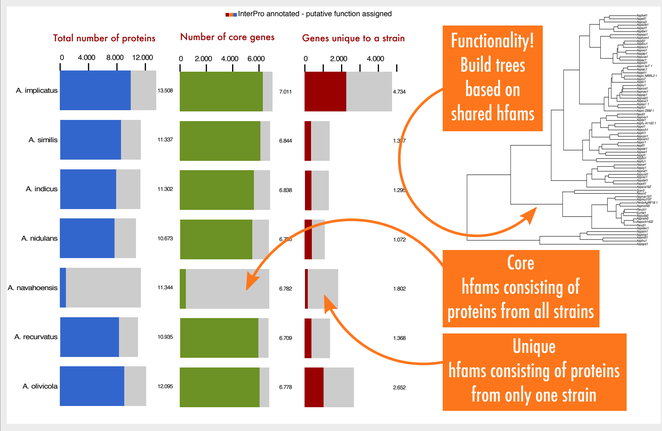
$$\textbf{Pairwise SMGC similarity score} = pident_{tailoring} * \frac{count_{tailoring}}{total_{tailoring}} * 0.35 + pident_{backbone} * \frac{count_{backbone}}{total_{backbone}} * 0.65$$



- SMGCs are predicted using the SMURF algorithm
- A costum score is used to calculate the similarity between clusters
- Two rounds of random walk clustering connectes the most similar clusters and creates a network which illustrates the interconnectedness of SMGCs

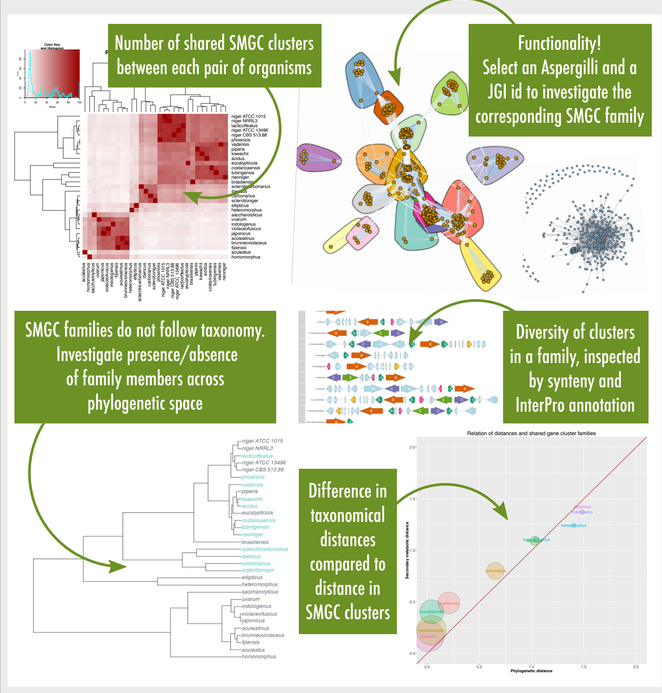
Genetic Diversity

- Analysis apps are available for analysis of genetic diversity through the construction of protein families - aspmine hfams
- DNA/protein sequence comparisons are essenitial to comparative genomcis
- Proteins with similar sequences form clusters of functinally related proteins - protein families
- Closely related strains share more families
- Many families are strain specific!



Secondary Metabolism

- Analysis apps are available for analysis of SMGC families and cluster variation across species of Aspergilli
- SMGC families can be quried using protein FASTA sequences or JGI protein identifiers
- Families can be inspected by synteny plots illustrating conserved functions and organization
- SMGC clusters do not follow the standard taxonomy and their presense across phylogeny can be explored



- Rshiny is a R package for interactive web apps
- Rshiny can be hosted on www.shinyapps.io
- Graphical interphases for R data and graphics
- Cheap hosting of interactive web-applications
- Analysis with customization and documentation
  - Hosted with www.shinyapps.io ($440 USD/year)
  - Unlimited apps, 500 active hours

aspmine.wordpress.com

Documentation

- Documentation of data analysis is often neglected
- Publication of thorough data methods is insufficient
- A webpage is a good place to document analysis
- The Asp Mine offers online documentation
- Access to analysis data and descriptions of methods